REMARKS

The Examiner is thanked for the courtesies extended during the telephonic interviews conducted with the undersigned on April 4 and June 15, 2005. As discussed below, the Examiner agreed that the claim amendments above overcome the rejections of the claims under 35 USC §§ 103 and 112, second paragraph.

Claim 10 has been amended to recite "pharmaceutical composition or a dietary supplement comprising from about 0.1 to about 1000 mg of phytanic acid or a derivative of phytanic acid." Support for this amendment is found in the specification at, for example, page 10, line 31 - page 11, line 21 and page 13, lines 1-4 and in original claim 1. *See*, *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claims 11-13 have been amended to delete "phytanic acid precursor...." In addition, claim 13 was amended to conform the Markush group. Support for these amendments is found in the specification at, for example, page 10, line 31 - page 11, line 21 and in original claims 11-13, respectively. *See id.*

Claims 20-24 have been added to recite various dosage ranges in the same manner as claim 10 has been amended. Support for these claims is found in the specification at, for example, page 13, lines 1-15 and Example 4 (page 20, lines 25-32). *Id.*

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Indefiniteness Rejection

Claims 10-13 were rejected under 35 USC § 112, second paragraph. (Paper No. 20050224 at 8.) In making the rejection, the Examiner asserted that claim 10 "reads on a combination of phytanic acid, a phytanic acid precursor and a derivative of phytanic acid into a single composition." (*Id.*)

Claim 10 has been amended to recite "phytanic acid or a derivative of phytanic acid...." Claims 11-13 have been amended to recite "the phytanic acid derivative...." As agreed, the amendments render the rejection moot and it should, therefore, be withdrawn.

Enablement Rejection

Claims 10-13 were rejected under 35 USC § 112, first paragraph. In making the rejection, the Examiner acknowledged that the specification is enabled for treating non-insulin dependent diabetes mellitus with phytanic acid. The Examiner asserted, however, that the specification "does not reasonably provide enablement for treating non-insulin dependent diabetes mellitus with a phytanic acid precursor or a derivative of phytanic acid or preventing non-insulin dependent diabetes mellitus with phytanic acid, a phytanic acid precursor, or a derivative of phytanic acid." (Paper No. 20050224 at 3.)

For the reasons set forth below, the rejection, respectfully is traversed.

As is well settled, it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry this burden, the Examiner must identify and clearly articulate the

factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370. "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, is it undue." MPEP § 2164.01 citing *In re Angstadt*, 190 USPQ 214, 219 (CCPA 1976).

Initially, we note that the rejection fails to make the requisite factual inquiry to support a conclusion that undue experimentation is required to make and/or use the claimed invention. In fact, the rejection has merely presented numerous conclusions as "facts" without any evidence or reasoning to support these conclusions.

For example, the Examiner asserts that "[t]here are no known preventive therapies for non-insulin dependent diabetes mellitus in the art"; "[i]t is clear the art to which the present invention relates is highly unpredictable and unreliable with respect to conclusions drawn from laboratory data extrapolated to clinical efficacy"; "the present invention is unpredictable unless experimentation is shown for a phytanic acid precursor or a derivative of phytanic acid to treat non-insulin dependent diabetes mellitus"; and "[c]urrent modes of treatment are known, but there are no known agents which can prevent non-insulin dependent diabetes mellitus." (Paper No. 20050224 at 5-6.) Each of these statements is simply a conclusion without any supporting evidence or reasoning.

Unsubstantiated conclusions, no matter how many, are not, and indeed cannot be, sufficient to support a *prima facie* case for lack of enablement. Absent the required ***factual*** analysis, it is respectfully submitted that the rejection should be withdrawn.

As discussed in the telephonic examiner interviews, the rejection has two bases: 1) the Examiner objected to the recitation of phytanic acid precursors and phytanic acid derivatives in the claims and 2) the Examiner objected to the recitation of "preventing" in the claims.

As to the first ground of rejection, the Examiner agreed that claims reciting phytanic acid or a derivative of phytanic acid would be allowable. Accordingly, claim 10 has been amended to recite "phytanic acid or a derivative of phytanic acid" and claims 11-13 have been amended to recite "a phytanic acid derivative." Accordingly, this basis of rejection has been rendered moot.

As to the second basis for rejection, the Examiner asserted that "[t]here are no examples showing the phytanic acid, phytanic acid precursors or derivatives of phytanic acid will, in fact, prevent non-insulin dependent diabetes mellitus especially in a human or an animal not presently at risk of or predisposed to developing such a disease or disorder." (Paper No. 20050224 at 6.) The Examiner also asserted that a "skilled artisan would expect that interaction of a particular agent in the prevention of NIDDM to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis of the agent." (*Id.* at 6-7.) "Absent reasonable *a priori* expectations of success, one skilled in the art would have to test extensively many conditions that may lead to NIDDM to discover which cause is prevented." (*Id.* at 7.) The Examiner then concluded that "[s]ince each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope." (*Id.*)

In an effort to further prosecution, attached hereto is a Declaration of Dr. Beat Flühmann, an inventor of the present invention, discussing the disclosure of the specification and knowledge in the art, and presenting additional experimental data that supports the disclosure in the specification that phytanic acid or a phytanic acid derivative will prevent NIDDM. Dr. Flühmann concludes that, as the specification makes clear, phytanic acid would be effective to treat or prevent NIDDM. (Declaration, ¶38.)

According to Dr. Flühmann the specification is replete with disclosure that supports the conclusion that phytanic acid, at physiological concentrations, acts via both peroxisome proliferator-activated receptors (PPAR) α and γ to activate the transcription of a distinct pattern of genes that favors glucose uptake and can be used to manage insulin resistance. (*Id.*, ¶6.) As Dr. Flühmann states "[t]hese *in vitro* and *in vivo* results confirm what is disclosed in the specification, namely that phytanic acid produces a biochemical result, which prevents or mediates the metabolic abnormalities associated with NIDDM *in vivo*." (*Id.*)

The Examples in the specification demonstrate that treatment with phytanic acid 1) increases the uptake of glucose in rat hepatocytes, 2) up regulates the production of the mRNA for various proteins related to glucose uptake (*e.g.*, GLUT-1, GLUT-2, glucokinase, and PEPCK), and 3) reduces plasma insulin levels. (*Id.*, ¶9.) As Dr. Flühmann observes, the specification discloses that these results demonstrate that administration of phytanic acid and phytanic acid derivatives normalize and increase the glucose level without a concomitant risk of hypoglycemia and is thus "excellently suited for the treatment or prevention of diabetes mellitus." (*Id.*, ¶7.)

To further support these disclosures, Dr. Flühmann conducted experiments demonstrating that administration of phytanic acid 1) induced a significant, dose-dependent stimulation of PPAR genes with a stronger selectivity PPAR-α and -γ compared to PPAR-β and 2) delayed onset of NIDDM in mice fed a high-fat diet. (*Id.*, ¶¶18-21, 31-34, and 37.)

Based on the disclosure in the specification and the relevant knowledge in the art, Dr. Flühmann concludes that "one skilled in the art would readily recognize that phytanic acid would be useful for treating or preventing non-insulin dependent diabetes mellitus." (*Id.*, ¶38.) "Moreover, the experimental results described above further confirm what was disclosed in the specification, namely that administration to a human or an animal of an effective dose of a pharmaceutical composition or a dietary supplement containing phytanic acid ... or a derivative of phytanic acid would be effective to treat or prevent non-insulin dependent diabetes mellitus." (*Id.*)

In sum, contrary to the Examiner's assertion, the specification clearly enables one of skill in the art to make and use the claimed invention. For this additional reason, it is respectfully submitted that rejection should be withdrawn.

Rejection under 35 USC § 103

Claims 10-13 were rejected under 35 USC § 103(a) as being unpatentable over Mukherjee, R., *et al.*, *Sensitization of diabetic and obese mice to insulin by retinoid X receptor agonists.* Nature, 386(6623), p. 407-10 (1997) ("Mukherjee") in view of Lemotte, *et al.*, *Phytanic acid is a retinoid X receptor ligand.* Eur J Biochem, 236(1), p. 328-33 (1996) ("Lemotte"). (Paper No. 20050224 at 9-10.)

For the reasons set forth below the rejection, respectfully is traversed.

Mukherjee discloses that:

> RXR agonists function as insulin sensitizers, markedly decreasing serum glucose, triglycerides and insulin in two animal models of insulin resistance. The combination of RXR and PPARγ ligands has additive or synergistic effects in stimulating transcription of and reducing the degree of hyperglycaemia and hypertrilyceridaemia in animal models of NIDDM. (Page 409.)

Lemotte discloses that phytanic acid is an agonist for RXRα and produces a conformation change in RXRα similar to that induced by retinoic acid. (Page 332.)

In making the rejection, the Examiner asserted that Mukherjee discloses that "retinoid X receptors are well-known to treat non-insulin dependent diabetes in mice (see the abstract). (Paper No. 10050224 at 10.) The Examiner acknowledged, however, that "the instant invention differs from [Mukherjee] in that [Mukherjee] does not teach the phytanic acid, a phytanic acid precursor, or a derivative of phytanic acid is preferred to treat non-insulin dependent diabetes mellitus." (*Id.*)

To fill the acknowledged gap, the Examiner relied upon Lemotte as disclosing "phytanic acid as a retinoid X receptor ligand." (*Id.*)

The Examiner then concluded that "one skilled in the art would have assumed that administration of phytanic acid to treat NIDDM is obvious since retinoid X receptors are well-know treat NIDDM in the absence of evidence to the contrary." (*Id.*)

Claim 10, the sole independent claim under examination, has been amended to recite that the phytanic acid or phytanic acid derivative is present in an amount "from 0.1 to 1000 mg." As agreed by the Examiner in the interviews, the cited

documents are completely devoid of any disclosure or suggestion of the claimed range. For this reason, the rejection has been rendered moot and should be withdrawn.

Moreover, we further note that the Examiner has identified no disclosure in either Mukherjee or Lemotte that discloses or suggests that the presently claimed method works through the action of phytanic acid on an RXR receptor. Indeed, as Dr. Flühmann observed, RXR and/or PPAR-α agonistic potential is not an indicator of a compounds anti-diabetic property. *See* Flühmann Decl. at ¶35. For this reason also, it is respectfully submitted that the rejection should be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 29, 2005.

Charles M. Avigliano

Charles M. Avigliano, Reg. No. 52,578

Respectfully submitted,

By: Charles M. Avigliano

Charles M. Avigliano
Registration No. 52,578
Stephen J. Brown
Registration No. 43,519
BRYAN CAVE LLP
1290 Avenue of the Americas
33rd Floor
New York, NY 10104-3300
Phone: (212) 541-2000
Fax: (212) 541-4630